REMARKS

Applicants respectfully request entry of the amendments and remarks submitted herein. Claims 21-32, 34-36, 38-43, 45-59, 61-63, and 65-71 are currently pending and under examination

I. The Rejection of the Claims under 35 U.S.C. § 102(b)

The Examiner rejected claims 21-26, 30-36, 39, 40, 42, 43, 45-53, 57-63, 66, 67 and 69-71 under 35 U.S.C. § 102(b), alleging that those claims are anticipated by Deggerdal *et al.* (WO 96/18731; hereinafter Deggerdal). As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

As amended, independent claim 21 recites a method for purifying RNA from biological material comprising RNA, comprising the steps of: (a) mixing said biological material with an RNA Lysing Solution buffered at a pH of greater than about 7, said RNA Lysing Solution comprising an amphiphillic reagent, and an RNA complexing salt, wherein the RNA-complexing salt is an alkali-metal salt present at a concentration greater than about 4 M, wherein said RNA Lysing Solution is free of a strong chaotropic substance; (b) lysing said biological material with said RNA Lysing Solution to form a lysate comprising nucleic acids comprising RNA and non-nucleic acid biological matter; (c) contacting said lysate to an immobilized non-silica solid support, wherein said nucleic acids comprising RNA in said lysate preferentially bind to said solid support; (d) washing said solid support with an RNA wash solution to remove non-nucleic acid biological matter; and (e) preferentially eluting the bound RNA from said solid support with an RNA elution solution to obtain the RNA. Claims 22-26, 30-36, 39, 40, 42, 43, and 46-48 depend directly or indirectly from claim 21.

As amended, independent claim 45 recites a method for purifying RNA from biological material, comprising the steps of: (a) contacting a biological material containing RNA with a solid support pre-treated with an RNA Lysing Solution buffered at a pH of greater than about 7, wherein the RNA Lysing Solution is bound to the solid support, said RNA Lysing Solution comprising an amphiphillic reagent and an RNA-complexing salt, wherein the RNA-complexing salt is an alkali-metal salt present at a concentration greater than about 4 M, wherein said RNA Lysing Solution is free of a strong chaotropic substance; (b) contacting said biological material

to said solid support in order to release nucleic acids comprising RNA and non-nucleic acid biological matter causing nucleic acids comprising RNA to preferentially bind to said solid support; (c) washing said solid support with an RNA wash solution to remove biological materials other than bound nucleic acids comprising RNA; and (d) preferentially eluting the bound RNA from said solid support with an RNA elution solution to obtain the RNA. Claims 49-53, 57-63, 66, 67 and 69-71 depend directly or indirectly from claim 45.

A rejection of anticipation under 35 U.S.C. § 102 requires the disclosure in a single prior art reference each element of the claim under consideration. *In re Dillon*, 919 F.2d 688, 16 U.S.P.Q.2d 1897, 1908 (Fed. Cir. 1990) (en banc), cert. denied, 500 U.S. 904 (1991). For anticipation, there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the art. *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 927 F.2d 1565, 18 USPQ2d 101 (Fed. Cir. 1991). To overcome the defense of anticipation, "it is only necessary for the patentee to show some tangible difference between the invention and the prior art." *Del Mar Engineering Lab v. Physio-Tronics, Inc.*, 642 F.2d 1167, 1172, (9th Cir. 1981). Applicants respectfully submit that the claims are not anticipated by the cited document.

As amended, independent claims 21 and 45 recite that the RNA-complexing salt in the RNA Lysing Solution is an alkali-metal salt present at a concentration greater than about 4 M, as was recited in previously-pending claims 37 and 64. As claims 37 and 64 were not included in the 35 U.S.C. § 102(b) rejection, Applicants respectfully request that the Examiner withdraw this rejection of the claims.

II. The Rejections of the Claims under 35 U.S.C. § 103(a)

The Examiner rejected claims 37, 38, 64 and 65 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Deggerdal in view of Wiggins (U.S. Patent No. 5,637,687; hereinafter Wiggins). The Examiner also rejected claims 41 and 68 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Deggerdal in view of the Calbiochem 2000-2001 reagent catalog (hereinafter Calbiochem). The Examiner also rejected claims 27-29 and 54-56 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Deggerdal in view of Heath *et al.* (WO 99/39009; hereinafter Heath). As these rejections may be maintained with respect to the pending claims, they are respectfully traversed.

The Supreme Court has set out the analysis for patentability under 35 USC 103(a): the scope and content of the cited documents are to be determined; differences between the cited documents and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. (*see, e.g., Graham v. John Deere Co.*, 383 U.S. 1 (1966) and *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007)) Further, the cited documents must be considered in their entirety, and it is not permissible to pick and choose from any one document only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such document fairly suggests to one of ordinary skill in the art. (*see, e.g., Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 230 U.S.P.Q. 416 (Fed. Cir. 1986) and *In re Wesslau*, 353 F.2d 238, U.S.P.Q. 391 (C.C.P.A. 1965)) Applicants submit that the level of ordinary skill in the pertinent art is high. The scope and content of the cited documents and the differences between the cited documents and the claims at issue are discussed hereinbelow, as are the reasons the claims are not obvious in view of the cited documents.

A. Deggerdal in view of Wiggins

The Examiner rejected claims 37, 38, 64 and 65 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Deggerdal in view of Wiggins.

The Examiner acknowledges that Deggerdal does not disclose a method in which lithium chloride is included in the lysis solution at a concentration of 4-10 M (see page 5 of the Office Action). As the Examiner acknowledges at page 4 of the Office Action, Deggardal does provide solutions in which lithium chloride is present at 0.5 M. Thus, Deggardal discloses a much lower concentration of LiCl (0.5 M) than the concentration of salt recited in the pending claims (greater than about 4 M). Further, Deggerdal goes so far as to state that "a salt may be included to enhance nucleic acid capture, although this is not necessary" (page 8, underline added). In contrast, the presently claimed methods recite the use of an RNA-complexing salt, which is an alkali-metal salt, at a concentration greater than 4 M, which is 8-fold greater than the optional salt concentration described by Deggerdal.

The Examiner alleges that Wiggins discloses the use of LiCl salt in a concentration of 2-5 M, preferably 4 M, citing to column 12, lines 25-35. Applicants respectfully point-out that the passage at column 12, lines 15-36 recites that "the first nucleic acid is precipitated by adding an

equal volume of an alcohol/salt solution" (underline added) and that the salt in the alcohol/salt solution is "present in a concentration of from about 2.0M to about 5.0M, more preferably about 4M." Example 4 is consistent with this language, as column 18, lines 38-43 recites, "[a]n equal volume of an isopropanol/salt solution comprising about 98 to 99% isopropanol and 4M LiCl was added to the aqueous phase to precipitate the RNA and dissolve the polysaccharides and other contaminants." When a volume of an alcohol/salt solution that has a concentration of 4M LiCl is added to an equal volume of a sample, the LiCl concentration in the resulting solution is 2M. Even if, for the sake of argument, LiCl is present in the alcohol/salt solution at the concentration of 5M, the final concentration would be 2.5M, which is well below the concentration recited in the pending claims.

Further, Wiggins relates to methods and compositions for isolating nucleic acids that involve the use of combinations of chaotropic agents (*see*, *e.g.*, the Abstract; column 6, lines 46-56; and column 6, line 63 through column 7, line 7). For isolating RNA, Wiggins teaches that the most preferred composition for isolating RNA uses three chaotropic agents (column 7, lines 11-14). Wiggins teaches that for isolating RNA, the pH of the solution is acidic, preferably from about 4 to 6, more preferably 5 (*see* column 9, lines 44-47).

Moreover, Applicants respectfully submit that it would not have been obvious for the art worker to modify Deggerdal by adding the use of a lithium chloride solution in accordance with Wiggins since Wiggins describes a very different isolation method from the instantly-claimed methods. While the instant claims are generally directed to methods utilizing bind-wash-elute methods, the isolation according to Wiggins generally proceeds via phase separation using a phenol-chloroform system and subsequent precipitation of the nucleic acid. The lithium chloride solution in the Wiggins procedure is not part of the lysis solution but instead of a precipitation solution. Thus, Applicants submit that the skilled person would not have expected that the lithium chloride solution in Wiggins would even be suitable in a process of the present invention.

Applicants respectfully submit that neither Deggerdal nor Wiggins teaches or suggests a method as claimed that involves the inclusion of an RNA-complexing salt that is an alkali-metal salt present at a concentration greater than about 4 M in the lysis buffer. Further, Wiggins relates to methods and compositions for isolating nucleic acids that involve the use of combinations of chaotropic agents. In contrast, the claims of the present invention recite that the RNA Lysing Solution is free of a strong chaotropic substance. Thus, Applicants respectfully submit that

Wiggins teaches away from excluding chaotropic agents from the lysing solution. Further, Wiggins teaches that for isolating RNA, the pH of the solution is acidic, preferably from about 4 to 6, more preferably 5, thereby teaching away from the use of an RNA lysing solution buffered at a pH of greater than about 7, as is presently claimed. Accordingly, the claims are not obvious in view of the cited documents, and Applicants respectfully request withdraw of this rejections of the claims under 35 U.S.C. § 103.

B. Deggerdal in view of Calbiochem

The Examiner rejected claims 41 and 68 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Deggerdal in view of the Calbiochem. Claim 41 depends indirectly from claim 21, and claim 68 depends indirectly from claim 45. As amended, independent claims 21 and 45 recite that the RNA-complexing salt in the RNA Lysing Solution is an alkali-metal salt present at a concentration greater than about 4 M, as was recited in previously-pending claims 37 and 64. As claims 37 and 64 were not included in this 35 U.S.C. § 103 rejection, Applicants respectfully request that the Examiner withdraw this rejection of the claims.

C. Deggerdal in view of Heath

The Examiner rejected claims 27-29 and 54-56 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Deggerdal in view of Heath. Claims 27-29 depend from claim 21, and claims 54-56 depend directly or indirectly from claim 45. As amended, independent claims 21 and 45 recite that the RNA-complexing salt in the RNA Lysing Solution is an alkali-metal salt present at a concentration greater than about 4 M, as was recited in previously-pending claims 37 and 64. As claims 37 and 64 were not included in the 35 U.S.C. § 103 rejection, Applicants respectfully request that the Examiner withdraw this rejection of the claims.

III. The Obviousness-Type Double Patenting Rejections of the Claims

The Examiner provisionally rejected claims 21-43 and 45-71 on the ground of nonstatutory obviousness-type double patenting, alleging that those claims are unpatentable over claims 1-85 of U.S. Application Serial No. 11/589,364. As this is a provisional obviousness-type double patenting rejection, Applicants will consider filing a terminal disclaimer should claims of the present application be found otherwise allowable.

The Examiner also provisionally rejected claims 21-25, 27-30, 46-50 and 52-55 under the judicially created doctrine of obviousness-type double patenting, alleging that those claims are unpatentable over claims 1 and 189 of U.S. Application Serial No. 09/154,830. U.S. Application Serial No. 09/154,830 has been abandoned (*see* the Notice of Abandonment mailed on July 03, 2007). Thus, Applicants request withdrawal of this rejection.

CONCLUSION

The Examiner is invited to contact Applicants' Representative at the below-listed telephone number if prosecution of this application may be assisted thereby. If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 50-3503. If any extensions of time are needed for timely acceptance of papers, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorize payment of any such extension fees to Deposit Account 50-3503.

Respectfully submitted,
Ellen M. Heath et al.
By their Representatives,
Viksnins Harris & Padys PLLP
Customer Number 53137
PO Box 111098
St. Paul, MN 55111-1098
(952) 8764094

Date: January 07, 2008

By: _____
Peter L. Malen
Reg. No. 44,894